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Range: from	begin to end Features: □SNP ☑CDD ☑MGC ☑HPRD ☑STS	tRNA Refresh
□1: <u>P08887</u>	7. Reports Interleukin-6 rec[gi:124343]	BLink, Conserved Domains, Links
Comment F	eatures Sequence	
LOCUS DEFINITION	P08887 468 aa linear PRI 07-FEB-2006 Interleukin-6 receptor alpha chain precursor (IL-6R-alpha) (IL-6R 1) (Membrane glycoprotein 80) (gp80) (CD126 antigen).	
ACCESSION VERSION DBSOURCE	P08887 P08887 GI:124343 swissprot: locus IL6RA_HUMAN, accession P08887; class: standard.	
	extra accessions:Q16202,Q53EQ7,Q5FWG2,Q5VZ23,created: Nov 1, 1988. sequence updated: Nov 1, 1988. annotation updated: Feb 7, 2006.	
	<pre>xrefs: X12830.1, CAA31312.1, X58298.1, CAA41231.1, AK223582.1, BAD97302.1, AL162591.16, CAH72853.1, BC089410.1, AAH89410.1, S72848.1, AAC60635.1, A41242, 1N26A, 1N2Q_C, 1N2Q_D, 1P9MC</pre>	
	xrefs (non-sequence databases): IntAct:P08887, Ensembl:ENSG00000160712, HGNC:6019, MIM: 147880, LinkHub:P08887, GO:0005576, GO:0005896, GO:0019899, GO:0004915, GO:0008283, GO:0007166, GO:0007275, GO:0006955, InterPro:IPR002996,	
	<pre>InterPro:IPR003961, InterPro:IPR003530, InterPro:IPR003599, InterPro:IPR007110, InterPro:IPR003598, Pfam:PF00041, Pfam:PF00047, SMART:SM00060, SMART:SM00409, SMART:SM00408, PROSITE:PS50853,</pre>	
KEYWORDS	PROSITE:PS01354, PROSITE:PS50835 3D-structure; Alternative splicing; Direct protein sequencing; Glycoprotein; Immunoglobulin domain; Membrane; Polymorphism; Receptor; Signal; Transmembrane.	
SOURCE	Homo sapiens (human)	
ORGANISM	<pre>Homo sapiens Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.</pre>	
REFERENCE	1 (residues 1 to 468)	
AUTHORS	Yamasaki,K., Taga,T., Hirata,Y., Yawata,H., Kawanishi,Y., Seed,B., Taniguchi,T., Hirano,T. and Kishimoto,T.	
TITLE	Cloning and expression of the human interleukin-6 (BSF-2/IFN beta 2) receptor	
JOURNAL PUBMED	Science 241 (4867), 825-828 (1988) 3136546	
REMARK	NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1).	
REFERENCE AUTHORS	Yamasaki,K., Taga,T., Hirata,Y., Yawata,H., Kawanishi,Y., Seed,B.,	
TITLE	Taniguchi,T., Hirano,T. and Kishimoto,T. Molecular structure of interleukin 6 receptor	
JOURNAL REMARK	Proc. Jpn. Acad., B, Phys. Biol. Sci. 64, 209-211 (1988) NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1).	
REFERENCE	3 (residues 1 to 468)	
AUTHORS	Schooltink, H., Stoyan, T., Lenz, D., Schmitz, H., Hirano, T., Kishimoto, T., Heinrich, P.C. and Rose-John, S.	
TITLE	Structural and functional studies on the human hepatic interleukin-6 receptor. Molecular cloning and overexpression in HepG2 cells	
JOURNAL PUBMED	Biochem. J. 277 (PT 3), 659-664 (1991) 1872801	
REMARK	NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1).	
REFERENCE AUTHORS	4 (residues 1 to 468) Totoki,Y., Toyoda,A., Takeda,T., Sakaki,Y., Tanaka,A. and Yokoyama,S.	
TITLE JOURNAL	Direct Submission Submitted (??-APR-2005)	

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REMARK
             NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 1).
             TISSUE=Kidney
REFERENCE
             5 (residues 1 to 468)
  AUTHORS
             Human chromosome 1 international sequencing consortium
  CONSRTM
  TITLE
             Direct Submission
             Submitted (??-MAY-2005)
  JOURNAL
             NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
  REMARK
REFERENCE
             6 (residues 1 to 468)
             Strausberg, R.L., Feingold, E.A., Grouse, L.H., Derge, J.G.,
  AUTHORS
             Klausner, R.D., Collins, F.S., Wagner, L., Shenmen, C.M., Schuler, G.D.,
             Altschul, S.F., Zeeberg, B., Buetow, K.H., Schaefer, C.F., Bhat, N.K.,
             Hopkins, R.F., Jordan, H., Moore, T., Max, S.I., Wang, J., Hsieh, F.,
             Diatchenko, L., Marusina, K., Farmer, A.A., Rubin, G.M., Hong, L.,
             Stapleton, M., Soares, M.B., Bonaldo, M.F., Casavant, T.L.,
             Scheetz, T.E., Brownstein, M.J., Usdin, T.B., Toshiyuki, S.,
             Carninci, P., Prange, C., Raha, S.S., Loquellano, N.A., Peters, G.J.,
             Abramson, R.D., Mullahy, S.J., Bosak, S.A., McEwan, P.J.,
             McKernan, K.J., Malek, J.A., Gunaratne, P.H., Richards, S.,
             Worley, K.C., Hale, S., Garcia, A.M., Gay, L.J., Hulyk, S.W.,
             Villalon, D.K., Muzny, D.M., Sodergren, E.J., Lu, X., Gibbs, R.A.,
             Fahey, J., Helton, E., Ketteman, M., Madan, A., Rodrigues, S., Sanchez, A., Whiting, M., Madan, A., Young, A.C., Shevchenko, Y.,
             Bouffard, G.G., Blakesley, R.W., Touchman, J.W., Green, E.D.,
             Dickson, M.C., Rodriguez, A.C., Grimwood, J., Schmutz, J., Myers, R.M.,
             Butterfield, Y.S., Krzywinski, M.I., Skalska, U., Smailus, D.E.,
             Schnerch, A., Schein, J.E., Jones, S.J. and Marra, M.A.
             Mammalian Gene Collection Program Team
  CONSRTM
             Generation and initial analysis of more than 15,000 full-length
  TITLE
             human and mouse cDNA sequences
  JOURNAL
             Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
   PUBMED
             12477932
             NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 2).
  REMARK
             TISSUE=Lymph
REFERENCE
                (residues 1 to 468)
             \label{eq:horiuchi,S., Koyanagi,Y., Zhou,Y., Miyamoto,H., Tanaka,Y., Waki,M., \\ \texttt{Matsumoto,A., Yamamoto,M.} \ \ \text{and Yamamoto,N.}
  AUTHORS
  TITLE
             Soluble interleukin-6 receptors released from T cell or
             granulocyte/macrophage cell lines and human peripheral blood
             mononuclear cells are generated through an alternative splicing
             mechanism
  JOURNAL
             Eur. J. Immunol. 24 (8), 1945-1948 (1994)
   PURMED
             8056053
             NUCLEOTIDE SEQUENCE [MRNA] OF 313-365 (ISOFORM 2).
  REMARK
REFERENCE
                (residues 1 to 468)
             Cole, A.R., Hall, N.E., Treutlein, H.R., Eddes, J.S., Reid, G.E.,
  AUTHORS
             Moritz, R.L. and Simpson, R.J.
             Disulfide bond structure and N-glycosylation sites of the
  TITLE
             extracellular domain of the human interleukin-6 receptor
  JOURNAL
             J. Biol. Chem. 274 (11), 7207-7215 (1999)
   PUBMED
             10066782
             PARTIAL PROTEIN SEQUENCE, CARBOHYDRATE-LINKAGE SITES, AND DISULFIDE
  REMARK
             BONDS.
REFERENCE
                (residues 1 to 468)
             Novick, D., Engelmann, H., Wallach, D. and Rubinstein, M.
  AUTHORS
  TITLE
             Soluble cytokine receptors are present in normal human urine
             J. Exp. Med. 170 (4), 1409-1414 (1989)
  JOURNAL
   PUBMED
             2529343
  REMARK
             PROTEIN SEQUENCE OF 20-49, AND SUBCELLULAR LOCATION.
REFERENCE
             10 (residues 1 to 468)
             Yawata, H., Yasukawa, K., Natsuka, S., Murakami, M., Yamasaki, K.,
  AUTHORS
             Hibi, M., Taga, T. and Kishimoto, T.
  TITLE
             Structure-function analysis of human IL-6 receptor: dissociation of
             amino acid residues required for IL-6-binding and for IL-6 signal
             transduction through gp130
  JOURNAL
             EMBO J. 12 (4), 1705-1712 (1993)
   PUBMED
             8467812
  REMARK
             MUTAGENESIS.
             11 (residues 1 to 468)
REFERENCE
             Martens, A.S., Bode, J.G., Heinrich, P.C. and Graeve, L.
  AUTHORS
  TITLE
             The cytoplasmic domain of the interleukin-6 receptor gp80 mediates
             its basolateral sorting in polarized madin-darby canine kidney
             cells
  JOURNAL
             J. Cell. Sci. 113 (PT 20), 3593-3602 (2000)
   PUBMED
             11017875
  REMARK
             FUNCTION.
             12 (residues 1 to 468)
REFERENCE
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Buk, D.M., Renner, O. and Graeve, L.
            Increased association with detergent-resistant membranes/lipid
 TITLE
            rafts of apically targeted mutants of the interleukin-6 receptor
            Eur. J. Cell Biol. 84 (10), 819-831 (2005)
 JOURNAL
            16270750
            FUNCTION, AND SUBCELLULAR LOCATION.
 REMARK
REFERENCE
            13 (residues 1 to 468)
 AUTHORS
           Varghese, J.N., Moritz, R.L., Lou, M.Z., Van Donkelaar, A., Ji, H.,
            Ivancic, N., Branson, K.M., Hall, N.E. and Simpson, R.J
 TITLE
            Structure of the extracellular domains of the human interleukin-6
            receptor alpha -chain
 JOURNAL
            Proc. Natl. Acad. Sci. U.S.A. 99 (25), 15959-15964 (2002)
            12461182
  PUBMED
 REMARK
            X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS) OF 20-344.
COMMENT
            On or before Dec 27, 2005 this sequence version replaced
            gi:74754774, gi:74755342, gi:74757093, gi:106829.
            [FUNCTION] Part of the receptor for interleukin 6. Binds to IL-6
            with low affinity, but does not transduce a signal. Signal
            activation necessitate an association with IL6ST. Activation may
            lead to the regulation of the immune response, acute-phase
            reactions and hematopoiesis.
            [FUNCTION] Low concentration of a soluble form of interleukin-6
            receptor acts as an agonist of IL6 activity.
            [SUBUNIT] Hexamer of two molecules each of IL6, IL6R and IL6ST.
            [INTERACTION] Q9NZ08:ARTS-1; NbExp=1; IntAct=EBI-299383,
            EBI-299412.
            [SUBCELLULAR LOCATION] Type I membrane protein (isoform 1);
            basolateral membrane. Secreted (isoform 2).
            [ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named
            isoforms=2; Name=1; Synonyms=Long; IsoId=P08887-1;
            Sequence=Displayed; Name=2; Synonyms=Short; IsoId=P08887-2;
            Sequence=VSP 001682, VSP 001683.
            [TISSUE SPECIFICITY] Isoform 2 is expressed in peripheral blood
            mononuclear cells and weakly found in urine and serum.
            [DOMAIN] The two fibronectin type-III-like domains, contained in
            the N-terminal part, form together a cytokine-binding domain.
            [DOMAIN] The WSXWS motif appears to be necessary for proper protein
            folding and thereby efficient intracellular transport and
            cell-surface receptor binding.
            [PTM] A short soluble form may also be released from the membrane
            by proteolysis.
            [SIMILARITY] Belongs to the type I cytokine receptor family. Type 3
            subfamily.
            [SIMILARITY] Contains 1 fibronectin type-III domain.
            [SIMILARITY] Contains 1 Ig-like C2-type (immunoglobulin-like)
            domain.
FEATURES
                     Location/Qualifiers
    source
                     1..468
                     /organism="Homo sapiens"
                     /db xref="taxon:9606"
                     1..468
    gene
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     Protein
                     1..468
                     /gene="IL6R"
                     /product="Interleukin-6 receptor alpha chain precursor"
    Region
                     1..19
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                     /region_name="Signal"
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                     recorded"
                     20..468
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                     /experiment="experimental evidence, no additional details
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                     /note="Interleukin-6 receptor alpha chain.
                     /FTId=PRO_0000010895."
    Region
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                     /inference="non-experimental evidence, no additional
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                /bond_type="disulfide"
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Region
                26..112
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                /experiment="experimental evidence, no additional details
                recorded'
                /note="Ig-like C2-type."
                32..33
Region
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                /region name="Hydrogen bonded turn"
                /experiment="experimental evidence, no additional details
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Region
                34..37
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                /region name="Beta-strand region"
                /experiment="experimental evidence, no additional details
                recorded"
                39..>96
Region
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                /note="IG_like"
                /db_xref="CDD: 5322"
                39..40
Region
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                43..46
Region
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Bond
                bond (47,96)
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Region
                48..49
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Region
                50
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                /region_name="Beta-strand region"
                /experiment="experimental evidence, no additional details
                recorded"
                52..53
Region
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Site
                55
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                /site_type="glycosylation"
                /experiment="experimental evidence, no additional details
                recorded"
                /note="N-linked (GlcNAc...)."
Region
                56..63
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                65..68
Region
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Region
                72..83
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                /region name="Beta-strand region"
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                85
Region
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Region
                88..90
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Region
                92..101
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Site
                93
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                103
Region
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                105..110
Region
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                120..125
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                recorded"
                bond(121,132)
Bond
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                /experiment="experimental evidence, no additional details
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Site
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Site
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                /site_type="mutagenized"
                /experiment="experimental evidence, no additional details
                /note="F->A: No change of ligand-binding and IL6
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Region
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                128
Region
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                /experiment="experimental evidence, no additional details
                recorded"
                130..134
Region
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                /region name="Beta-strand region"
                /experiment="experimental evidence, no additional details
                recorded"
Site
                132
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Region
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Site
                140
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                /site_type="mutagenized"
                /experiment="experimental evidence, no additional details
                recorded"
                /note="P->G: No change of ligand-binding and IL6
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Region
                142..143
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                recorded"
Region
                145..157
                /gene="IL6R"
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                /experiment="experimental evidence, no additional details
                recorded"
Site
                153
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                /experiment="experimental evidence, no additional details
                /note="F->L: No change of ligand-binding and IL6
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                159..168
Region
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Bond
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Site
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                /site_type="mutagenized"
                /experiment="experimental evidence, no additional details
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Region
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Region
                173..178
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Site
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                signaling."
Site
                176
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                /experiment="experimental evidence, no additional details
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Site
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                190
Site
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                /experiment="experimental evidence, no additional details
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Site
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Region
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                206..209
Region
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                210..212
Region
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                210
Region
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Site
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Region
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Region
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Region
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Region
                231..232
                /gene="IL6R"
                /region_name="Hydrogen bonded turn"
                /experiment="experimental evidence, no additional details
                recorded"
Site
                232
                /gene="IL6R"
                /site_type="mutagenized"
                /experiment="experimental evidence, no additional details
                recorded"
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                233
<u>Site</u>
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                /note="W->Q: 30% decrease of ligand-binding and increase
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                234..239
Region
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                recorded"
                242..243
Region
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                /region name="Hydrogen bonded turn"
                /experiment="experimental evidence, no additional details
                recorded"
Site
                245
                /gene="IL6R"
                /site type="glycosylation"
                /experiment="experimental evidence, no additional details
                recorded"
                /note="N-linked (GlcNAc...)."
                247..249
Region
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                /region_name="Beta-strand region"
                /experiment="experimental evidence, no additional details
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Region
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                /experiment="experimental evidence, no additional details
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Site
                254
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Region
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recorded"
                263
Region
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Region
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                recorded"
                271..273
Region
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                recorded"
                275..281
Region
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                277
Site
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                /experiment="experimental evidence, no additional details
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                /note="C->D: 30% increase of ligand-binding and 100%
                increase in IL6 signaling."
Site
                278
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                /experiment="experimental evidence, no additional details
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                /note="V->N: 50% Decrease of ligand-binding and 50%
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Site
                279
                /gene="IL6R"
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                /experiment="experimental evidence, no additional details
                /note="I->D: Complete loss of ligand-binding."
Site
                280
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                /site_type="mutagenized"
                /experiment="experimental evidence, no additional details
                recorded"
                /note="H->I: No change of ligand-binding and no IL6
                signaling."
Site
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                /site_type="mutagenized"
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                /note="D->G: 70% decrease of ligand-binding and no IL6
                signaling."
Region
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                /region name="Hydrogen bonded turn"
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                recorded"
Site
                285
                /gene="IL6R"
                /site_type="mutagenized"
                /experiment="experimental evidence, no additional details
                recorded"
                /note="G->D: 80% decrease of ligand-binding and no IL6
                signaling."
Region
                288..296
                /gene="IL6R"
                /region name="Beta-strand region"
                /experiment="experimental evidence, no additional details
                recorded"
Site
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                /gene="IL6R"
                /site type="mutagenized"
                /experiment="experimental evidence, no additional details
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/note="Q->K: Complete loss of ligand-binding."
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                      /note="R->G: Complete loss of ligand-binding."
     Region
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                      /gene="IL6R"
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     Region
                      300..301
                      /gene="IL6R"
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                      303..307
     Region
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                      /experiment="experimental evidence, no additional details
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                      /note="WSXWS motif."
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                      356..365
     Region
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                      /experiment="experimental evidence, no additional details
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                      358
                      /gene="IL6R"
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                      /experiment="experimental evidence, no additional details
                      /note="D -> A (in dbSNP:8192284). /FTId=VAR_021995."
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                      366..468
                      /gene="IL6R"
                      /region name="Splicing variant"
                      /experiment="experimental evidence, no additional details
                      recorded"
                      /note="Missing (in isoform 2). /FTId=VSP_001683."
                      366..386
     Region
                      /gene="IL6R"
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                      /inference="non-experimental evidence, no additional
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                      /note="Potential."
                      387..468
     Region
                      /gene="IL6R"
                      /region_name="Topological domain"
                      /inference="non-experimental evidence, no additional
                      details recorded"
                      /note="Cytoplasmic (Potential)."
ORIGIN
        1 mlavgcalla allaapgaal aprrcpaqev argvltslpg dsvtltcpgv epednatvhw
       61 vlrkpaagsh psrwagmgrr lllrsvqlhd sgnyscyrag rpagtvhllv dvppeepqls
      121 cfrksplsnv vcewgprstp slttkavllv rkfqnspaed fqepcqysqe sqkfscqlav
      181 pegdssfyiv smcvassvgs kfsktqtfqg cgilqpdppa nitvtavarn prwlsvtwqd
      241 phswnssfyr lrfelryrae rsktfttwmv kdlqhhcvih dawsglrhvv qlraqeefgq
      301 gewsewspea mgtpwtesrs ppaenevstp mgalttnkdd dnilfrdsan atslpvqdss
361 svplptflva ggslafgtll ciaivlrfkk twklralkeg ktsmhppysl gglvperprp
      421 tpvlvplisp pvspsslgsd ntsshnrpda rdprspydis ntdyffpr
//
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